I Claim

1. A method of treating neoplasm in a mammal in need of such treatment, comprising administering to said mammal a therapeutic agent comprising venom and/or mammalian, plant or insect anti-serum reactive with at least one Phospholipase A_2 enzyme.

2. A method according to claim 1 wherein the anti-serum is reactive with two or more Phospholipase A_2 type enzymes.

3. A method according to claim 1 wherein the at least one Phospholipase A_2 Type enzyme is Type I, Type II, Type III or Type IV.

4. A method according to claim 1 wherein the anti-serum is either polyclonal or monoclonal.

5. A method of treating a mammal prophylactically to prevent neoplastic development, comprising administering to said mammal a therapeutic vaccine containing venom and/or mammalian, plant or insect PLA_2 enzymes or part thereof as the principal antigen component.

6. A pharmaceutical formulation containing venom and/or mammalian plant or insect anti-serum to PLA_2 enzyme or part thereof in combination with anti-serum to Phospholipase C enzyme or part thereof or inhibitory compounds to Phospholipase C for use as a therapeutic agent for the therapy of a neoplastic condition in a human or animal.

7. A method according to claim 6 wherein the inhibitory compounds to Phospholipase C is one or more of EDTA, Phenanthroline, Chloromercuribenzoic Acid, Iodoacetic Acid, and I-oleoyl-2-acetyl-sn-glycerol(OAG).

8. A pharmaceutical formulation containing one or more venoms or venom components as antigen and/or mammalian, plant or insect PLA_2 enzyme as antigen in combination with Phospholipase C enzyme.

9. A method according to Claim 8 wherein the phospholipase C enzyme inhibitor is used in combination with the therapeutic agents of Claim I to enhance anti neoplastic and anti metastatic activity.

10. A method according to any one of Claims 1, 5, 6 and 8, wherein the administration is part of a combination therapy with other therapeutically effective agents.

11. A method according to Claims 1, 5, 6 and 8 wherein the administration is in combination with adjuvants.

12. A method according to Claims 1, 5, 6 and 8 wherein the venom is that of snakeand/or insect.

13. A method according to Claims 1, 5, 6 and 8 wherein the Phospholipase A_2 enzyme showing Phospholipase A_2 activity is obtained from more than one species of snake and/or insect, mammal or plant.

14. A method according to Claims 1, 5, 6 and 8 wherein the therapeutic agent is administered as an anti-inflammatory agent.

15. A method according to Claims 1, 5, 6 and 8 wherein the therapeutic agent is administered to prevent the occurrence of immunosuppression.

16. A method according to Claims 1, 5, 6 and 8 wherein the therapeutic agent is administered in the treating of allergic contact dermatitis, Asthma and Psoriasis and bronchitis.

17. A method according to Claims 1, 5, 6 and 8 wherein the anti-serum is administered for the treatment of physiological condition resultant from elevated levels of phospholipase A_2 products and/or metabolites.

18. A method according to claim 17 wherein the physiological condition is Schizophrenia.

19. A method according to Claims 1, 5, 6, 8 and 17 wherein the anti-serum to Phospholipase A_2 and/or C are produced synthetically by molecular imprinting of template organic molecules using these enzymes.

20. Therapeutic agents according to Claims 1, 5, 6 and 8 for treating one or more of the following:- Rheumatoid arthritis, osteoarthritis, gout, rheumatic carditis and autoimmune diseases, allergic diseases, bronchial asthma, septic shock, renal failure, pancreatis, myasthenia gravis and ocular and dermal inflammatory diseases, psoriasis, splenomegaly, cancer, metastatic spread of neoplasm, collagen vascular disease, myocardial ischemia, cellular

chemotaxis, depression, erythema, vascular permeability resultant from enhanced production of PGE_2, acne, atopic diseases, malaria, allergic conjunctivitis, schizophrenia, reiters syndrome, raynaud's phenomenon, lupus, Chron's and Graves disease.

21. A method according to Claims 1, 5, 6, 8 and 17 wherein the Fc receptor of the antibody to either Phospholipase A_2 and C used in this therapeutic method is either totally or partially removed.

22. A method according to Claims 6, 8, 19 and 21 wherein a non-toxic compound demonstrating inhibiting activity against Phospholipase C enzymes may be utilised in conjunction with the PLA_2 anti-serum to enhance its anti-neoplastic (tumour) and anti-metastatic activity.

23. A method according to Claims 1, 5, 6, 8,17 and 19 wherein the anti-serum is generated to human Phospholipase A_2 enzyme either in a mono and/or polyclonal form.

24. A method according to Claims 1, 5, 6, 8 and 17 wherein the anti-serum to Phospholipase A_2 enzyme is generated in eggs, producing antibodies which do not react with the human Compliment system.

25. A method according to Claims 1, 5, 6, 8 and 17 wherein the anti-serum to venom, mammalian, plant or insect Phospholipase A_2 is generated in mammals and extracted from the colostrum and preferably but not essentially affinity purified for use in oral administration to patients either alone or in combination with anti-serum similarly produced to human Phospholipase C enzyme components.

26. A method of inoculation of human or animal with a combination of two or more phospholipase A_2 enzymes types.

27. A method according to claim 26 where the antibody response to the inoculation confers prophylactic and/or therapeutic benefit to patient.

28. A method according to claim 27 wherein the patient is in need of a treatment for a neoplastic condition.

29. A method according to claims 26, 27 and 28 wherein the phospholipase A_2 type is Type I, Type II, Type III or Type IV.

30. A method according to claim 29 wherein the Phospholipase A_2 is obtained from venom.

31. A method according to claim 29 wherein the Phospholipase A_2 is obtained from animal or plant species.

32. A method according to claim 1, 5, 6, 8 and 26 wherein the phospholipase A_2 is synthetically produced or cloned.

33. A method of early detection of neoplastic disease by utilising the detection of enhanced PLA_2 levels in patients.

34. A method according to claim 33 wherein the detection of enhanced PLA_2 is established by the use of Lipose Diagnostic Kit.

35. A method according to claims 2, 26, 27 and 28 wherein Phospholipase A_2 type enzyme has a size of between 40-80 kDa.

36. A method of targeting cancer cells by use of Type I and/or Type II PLA_2 as targeting agent with hydrophilic tail.

37. A method according to claim 36 wherein the targeting agent is a liposome containing anti-serum to PLA_2 or conventional chemotherapy drugs.

38. A method treating parasitic and bacterial infections in mammals by the administration of a therapeutic agent containing venom and/or mammalian, plant or insect anti-serum reactive with Phospholipase A_2 enzymes

39. A method according to Claim 38 wherein the anti-serum is reactive with one or more Phospholipase A_2 type enzymes

40. A method according to Claim 39 wherein the Phospholipase A_2 Type enzymes is one of Type I, Type II, Type III or Type IV.

41. A method according to Claim 38 wherein said parasite is an haemoflagellate parasite.

42. A method as recited in Claim 41 wherein said parasite is a member of the group of haemoflagellate parasites consisting of Leishmania, Trypanosomia and Toxoplasma.

ABSTRACT

The present invention comprises the method of treating a host organisms (man or animal) in need of a drug having direct or prophylactic anti-neoplastic activity comprising the administration of a therapeutically effective amount of Phosphohpase A_2 targeted venom anti-serum alone or in combination with a known Phospholipase C anti-serum or a Phospholipase C inhibitory compound. A vaccine containing in whole or in part snake or insect venom or mammalian PLA_2 components comprising epitopes demonstrating Phospholipase A_2 activity and/or Phospholipase C enzyme components. This patent presents therapeutic pharmaceutical formulations containing snake and/or insect venoms, or extracts from such venoms which contain, total or partial, phospholipase A_2 enzyme activity or PLA_2 epitopes. This patent presents therapeutic pharmaceutical formulations containing anti-serum to snake and/or insect venoms and/or mammalian PLA_2 enzymes wherein the anti-serum has been preferably affinity purified for use in treating patients suffering from neoplastic disease. This patent presents pharmaceutical formulations containing organic polymer mimic molecules generated to snake and/or insect venoms or the PLA_2, enzyme components thereof and/or PLA_2 enzymes isolated from insect, mammalian on plant cells, and/or Phospholipase C enzyme preparation or extract from such venoms which may contain, total or partial, phospholipase A_2 enzyme activity.

In this patent the affinity purified anti-serum to venoms Phospholipase A_2 (PLA_2) and mammalian or plant PLA_2 are shown to be active anti-proliferative neoplastic agents.

The present invention comprises the method of treating host organisms (i.e. human or animal) in need of a drug having anti-neoplastic activity comprising the administration of a therapeutically effective amount of venom anti-serum either alone or preferably in combination with a Phospholipase C inhibitor of non-toxic nature or monoclonal or polyclonal anti-serum to Phospholipase C enzyme or a vaccine containing in whole or in part venom

and/or other components of animal, insect or plant origin showing Phospholipase A_2 and/or Phospholipase C activity. This patent presents pharmaceutical formulations containing snake and/or insect venoms, or extracts from such venoms which may contain, total or partial, Phospholipase A_2 enzyme activity alone or in combination with animal or plant Phospholipase A_2 with or without Phospholipase C inhibiting compounds or Phospholipase C mono or polyclonal anti-serum to Phospholipase C enzyme as therapeutic vaccine candidate for all neoplastic diseases. This patent presents therapeutic pharmaceutical formulations containing anti-serum to snake and/or insect venoms wherein the anti-serum is preferably affinity purified for use in treating neoplastic diseases. This patent presents pharmaceutical formulations containing organic polymer mimic molecules generated to snake and/or insect and/or mammalian and/or plant PLA_2 enzymes or epitopes, or extract from such venoms or synthetic peptides and/or other molecules which may contain, total or partial, Phospholipase A_2 and C enzyme activity.

Phospholipase A_2 are lipolytic enzymes that hydrolyze the sn-2-acylester bond in glycerophospholipids. Many forms of PLA_2 exist in nature and have been described and classified into several groups. Types I, II and III PLA_2 are low molecular weight peptides (13-18 kDa) extra-cellular enzymes, including pancreatic and cobra venom PLA_2 (type I), rattle snake and inflammatory PLA_2 (type II) and bee venom type III. Intracellular cytosolic PLA_2 belong to different groups, including the 85 kDa (type IV) and 40-75 kDa enzymes.

Affinity purified anti-serum to venoms, animal or plant tissue demonstrating the ability to bind PLA_2 enzymes are shown herein below, by way of example, to be active in-vitro and in-vivo anti-proliferative neoplastic agents. Accordingly, these affinity purified antisera either alone or in combination with non-toxic Phospholipase C inhibitor or anti-serum to Phospholipase C are useful in the control of proliferation of neoplastic tissue.